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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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YOUNG & THOMPSON
745 SOUTH 23RD STREET 2ND FLOOR
ARLINGTON, VA 22202

EXAMINER

KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 05/29/2003

27

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/380,086

Applicant(s)

PEREZ ET AL.

Examiner

Anne R. Kubelik

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 March 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

1. As requested in Paper No. 26, filed 20 March 2003, the claims 13-18 have been cancelled, and claims 19-26 have been added. Claims 19-26 are pending.
2. As art has been found on both Groups I and II, the restriction between those two groups is withdrawn.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

4. Claims 22-24 and 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 20 September 2002, as applied to claims 13-16 and 18. Applicant's arguments filed 20 March 2003 have been fully considered but they are not persuasive.

Applicant urges that the Office action fails to provide evidence for the contention that the specification does not provide guidance for transforming a male sterile plant with a transgene or integrating a transgene genetically linked to an AMS gene into a male sterile plant. Applicant urges that Worral et al, cited in a previous action, teaches these, and that classical methods for introducing a transgene into a plant are taught in the specification on pg 10-11 and examples 3 and 4 (response pg 3-5).

This is not found persuasive. Claim 22 is drawn to a method that reads on transforming a

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plant with a transgene such that the transgene is genetically linked to an AMS gene. While transformation with a construct that comprises both the transgene and an AMS is enabled, targeted transformation such that a transgene is transformed to an AMS already present in a plant is not enabled. The specification fails to provide guidance for a method of transformation to target the transgene to the region of the nuclear genome near the gene responsible for the artificial male sterility.

See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that disclosure of a “mere germ of an idea does not constitute [an] enabling disclosure”, and that “the specification, not the knowledge of one skilled in the art” must supply the enabling aspects of the invention.

Applicant urges that new claim 22 is drawn to a method wherein a transgene of interest is genetically linked with an AMS gene. Applicant urges that examples 1 and 2 describe construction of vectors encoding PR glucanase, barnase or dog gastric lipase; the first two confer AMS, while the third is a transgene of interest (response pg 5-6).

This is not found persuasive for the reasons above.

5. Claims 19-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 20 September 2002, as applied to claims 13-16 and 18. Applicant's arguments filed 20 March 2003 have been fully considered but they are not persuasive.

Applicant urges that the specification on pg 3, lines 33-35 states that male sterility is used

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to produce a transgenic plant or a part thereof and that the specification on pg 4, lines 5-6 states that parts include fruits. Applicant also urges that maize is an example of a plant of the invention, as stated on pg 4, lines 38 and on. Applicant urges that the specification on pg 4, lines 38-39 states that in the case of maize, seed production is discussed, and that the specification on pg 5, lines 30-31, states that male sterile transgenic plants are used by seed companies to facilitate seed production (response pg 6-7).

This is not found persuasive because none of these states that the invention is limited to use in plants that are cultivated for seed or fruit production as opposed to plants cultivated for other uses. Pg 3, lines 33-35 and pg 4, lines 5-6 state that the invention is a fruit of a plant in which a transgene of interest is genetically linked to an AMS gene; it does not state that the invention is limited to use in plants that are cultivated for seed or fruit production. The paragraph spanning pg 4-5 explains how seed can be produced from male sterile maize, and thus does not provide support for limiting the use of the method to plants cultivated for seed or fruit production. Pg 5, lines 30-31 of the specification is directed to common use of CMS plants; it does not state that the method is to be only used on plants cultivated for seed or fruit production.

Applicant urges that the specification on pg 6, lines 12-18, also describes a method for seed or fruit production comprising pollinating male sterile plants and harvesting the females, that is fertilized male sterile plants that therefore produce seed or fruit (response pg 7).

This is not found persuasive because pg 6, lines 12-18, is directed to methods for how to overcome production problems in the male sterile plants, but does not state that the method is to be only used on plants cultivated for seed or fruit production.

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6. Claims 19-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is repeated for the reasons of record as set forth in the Office action mailed 20 September 2002, as applied to claims 13-16 and 18. Applicant's arguments filed 20 March 2003 have been fully considered but they are not persuasive.

Applicant urges the claims have been amended, making these rejections moot (response pg 7-8). This is not found persuasive because the following rejections remain or are new:

Claims 19 and 22 are indefinite in their recitation of "incorporating said transgene". The use of this phrase, which modifies "transgenic plant" makes it seem that the plant is in the process of active incorporation of the transgene. It is suggested that the phrase be amended to indicate that the transgene is already incorporated into the genome of the plant.

Claims 19 and 22 are indefinite in their recitation of the phrase starting with "comprising" in line 3. It is not clear what this phrase is intended to modify - the transgene? the plant? the method? By position in the claim, the phrase modifies the transgene. If Applicant wishes it to modify "method", it is suggested that "comprising" be replaced with --wherein the method comprises--.

It is suggested that for clarity --and-- be inserted before "wherein" in claim 19, line 6, and claim 22, line 8.

Claim 22 is indefinite in its recitation of "artificial male sterility (AMS) gene" in lines 6-7. It is unclear what it means for a male sterility gene to be artificial - in what manner is it artificial?

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Claim 22 is indefinite in its recitation of “genetically linked” in line 6. Does this mean the AMS gene is on the plasmid vector or does this mean that only after transformation is the transgene is linked to the AMS gene?

Claim Rejections - 35 USC § 102

7. Claims 19 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Svab et al (1990, Proc. Natl. Acad. Sci. USA 87:8526-8530). The rejection is repeated for the reasons of record as set forth in the Office action mailed 20 September 2002, as applied to claim 13. Applicant’s arguments filed 20 March 2003 have been fully considered but they are not persuasive.

Svab et al teach transformation of a male sterile tobacco plant with a transgene that confers spectinomycin resistance (pg 8526, right column, paragraph 1, and pg 8527, right column, paragraph 1). This method would inherently prevent dissemination by pollen, because the plants are male sterile. Tobacco is cultivated for seed production, for example for planting. The spectinomycin resistance gene encodes a compound that is therapeutic or prophylactic for the plant.

Applicant urges that the tobacco plant disclosed in Svab fails to carry cytoplasmic male sterility or an AMS gene. Applicant urges that the plants are functionally male sterile because of shortened filaments but are capable of producing viable pollen by hand pollination. Applicant urges pg 4, lines 27-34 of the specification states that male sterility of the invention is an artificial genic male sterility that renders the transgenic plant unable to produce viable pollen (response pg 8-9).

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This is not found persuasive. The plants taught by Svab et al do not produce pollen due to being functionally male sterile, but are hand pollinated using pollen from a male fertile plant. They cannot be used to pass the transgene from one generation to the next. Official notice is taken of the following facts that are well-known in the art: In tobacco "cytoplasm" is only transmitted via the egg; the pollen does not possess mitochondria and plastids and thus does not possess the CMS gene. Thus, in order to produce progeny plants that contain the CMS gene, the plants must be used as the female parent in a cross. Therefore, the manual pollination discussed in Svab is not done using pollen from Nt(pbg). It is also noted that because plastids are only transmitted via the egg, the plastid transformed plants taught by Svab would be inherently unable to transmit the transgene even if they were not already male sterile.

The specification does not define male sterility as artificial genic male sterility that renders the transgenic plant unable to produce viable pollen. The cited lines merely state that plants containing a particular AMS are unable to produce viable pollen.

8. Claims 19 and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Maliga et al (1995, US Patent 5,451,513). The rejection is modified from the rejection set forth in the Office action mailed 20 September 2002, as applied to claim 13. Applicant's arguments filed 20 March 2003 have been fully considered but they are not persuasive.

Maliga et al teach transformation of a male sterile tobacco plant with a transgene that confers spectinomycin resistance (column 12, line 63, to column 13, line 4, and column 14, lines 21-31). This method would inherently prevent dissemination by pollen, because the plants are male sterile. Tobacco is cultivated for seed production, for example for planting. The spectinomycin resistance gene encodes a compound that is therapeutic or prophylactic for the

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plant. Furthermore, Maliga et al teach the production of therapeutic proteins like insulin in the plastids (column 9, lines 25-30).

Applicant urges that the tobacco plant disclosed in Maliga fails to carry cytoplasmic male sterility or an AMS gene. Applicant urges that the plants are functionally male sterile because of shortened filaments but are capable of producing viable pollen by hand pollination. Applicant urges pg 4, lines 27-34 of the specification state that male sterility of the invention is an artificial genic male sterility that renders the transgenic plant unable to produce viable pollen (response pg 8-9).

This is not found persuasive for the reasons discussed above in the rejection of Svab et al.

9. Claims 22-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Jorgensen (1993, US Patent 5,180,873). The rejection is repeated for the reasons of record as set forth in the Office action mailed 20 September 2002, as applied to claims 13-16 and 18. Applicant's arguments filed 20 March 2003 have been fully considered but they are not persuasive.

Jorgensen teaches a method of introducing a transgene (for example, a kanamycin resistance gene) into a plant by transformation (column 16, line 1, to column 18, line 68; column 19, line 40, to column 23, line 8; claims 1-40), wherein the plant is maize, rapeseed or tomato (column 7, lines 45-62; column 17, lines 7-28; and column 19, line 40, to column 23, line 8, claim 19). The transformants are male sterile and contain the transgene. The male sterility would "artificial" because it is caused by mutation. This method is one where the transgene is "genetically linked" to the male sterility gene (column 22, lines 40, to column 23, line 8; claims 1-40). This method would inherently be one for preventing dissemination of a transgene via pollen because the transformed male sterile plants would not be able to produce pollen (column

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18, lines 57-68) and thus, the transgene could not be disseminated by pollen. The kanamycin resistance gene encodes a compound that is therapeutic or prophylactic for the plant.

Applicant urges that Jorgensen states that in crops in which the product depends on fertilization, CMS can only be used if a restorer gene is available to restore fertility and that dominant sterile alleles can be used in crops where seed is not an important product (response pg 9-10).

This is not found persuasive because this is true of the instant invention as well. As one of skill in the art would know, Jorgensen's statement that CMS can only be used if a restorer gene is available to restore fertility refers to the fact that CMS plants are not self-fertile and will not produce fertile progeny; thus, selfed progeny or fertile progeny are desired, a fertility restorer must be used. However, one of skill in the art would know that if one wants non-fertile progeny, a restorer gene is not required.

Jorgensen's statement about dominant sterile alleles discusses inherent properties of certain kinds of nuclear male sterility and would apply to the instant application as well.

In response to applicant's argument that the reference fails to show certain features of applicant's invention, it is noted that the features upon which applicant relies (*i.e.*, dominant sterile alleles) are not recited in the rejected claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant urges that Jorgensen describes a method for producing transgenic plants with a marker closely linked to a nuclear male sterile locus and not transforming a plant with a transgene and an AMS gene at the same time or wherein the AMS gene is linked to the transgene (response pg 10-11).

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This is not found persuasive. By Applicant's admission, the AMS gene is genetically linked to the transgene because the marker is closely linked to a nuclear male sterile locus. Note that the specification does not define "genetically linked" as "immediately adjacent to one another; in the art "genetically linked" has a broad range of meanings, and two genes are genetically linked even if they are on opposite ends of the same chromosome.

In response to Applicant's argument that the reference fails to show certain features of applicant's invention, it is noted that the features upon which Applicant relies (*i.e.*, transforming a plant with a transgene and an AMS gene at the same time) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

10. Claims 22-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Mariani et al (US Patent 5,689,041, filed March, 1991). The rejection is repeated for the reasons of record as set forth in the Office action mailed 20 September 2002, as applied to claims 13-16. Applicant's arguments filed 20 March 2003 have been fully considered but they are not persuasive.

Applicant urges that Mariani describe a fertility restorer plant and method wherein a male sterile plant is crossed to the restorer plant. Applicant believes the method is limited to crossing of plants with nuclear male sterility and urges that progeny resulting from the cross cannot prevent pollination (response pg 11-12).

This is not found persuasive because Mariani et al states that 25% of the plants are male sterile (column 28, lines 16-19). These plants thus do prevent dissemination by pollen. Furthermore, the kanamycin resistance gene would be therapeutic or prophylactic for the plant.

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11. Claims 22-24 are rejected under 35 U.S.C. 102(e) as being unpatentable over Fabijanski et al (US Patent 5,728,558, filed July, 1990). The rejection is modified from the rejection set forth in the Office action mailed 20 September 2002, as applied to claims 13-16. Applicant's arguments filed 20 March 2003 have been fully considered but they are not persuasive.

Fabijanski et al teach a method of producing male sterile Brassica napus (rape) or tobacco plants by transforming the plants a gene that confers artificial male sterility, wherein the gene is "genetically linked" to a gene of interest like hygromycin or kanamycin resistance (examples 2-34; claims 1 and 3-10). The male sterility gene would be nuclear, because it is transformed into the nucleus, and it would be artificial. This method would inherently be one for preventing dissemination of a transgene via pollen because the transformed male sterile plants would not be able to produce pollen, and thus, the transgene could not be disseminated by pollen. The hygromycin or kanamycin resistance genes encode compounds that would be therapeutic or prophylactic for the plant. Tobacco and rape would be cultivated for seed production, for example for planting.

Applicant urges that Fabijanski et al is drawn to a recombinant DNA molecule for preparation of a male sterile plant along with the use of the plant to produce hybrid seeds. Applicant urges that the cited paragraphs do not refer to a transgenic plant carrying an AMS gene in conjunction with a transgene of interest, but relates to a plant carrying two genes that are non-genetically linked. Applicant urges that Fabijanski et al state that two recombinant DNA molecules are necessary to interfere with the function and development of a cell (response pg 12-13).

This is not found persuasive because the rejection has been modified as above.

Applicant believes that the rejection of Fabijanski et al in view of each of Ellstrand et al

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and Nyers et al has been maintained and repeats the above with respect to Fabijanski et al.

Applicants thus urges that it cannot be stated that Fabijanski et al would inherently disclose the prevention of transgene escape. Applicant also urges that Nyers et al and Ellstrand et al fail to actually use male sterility to prevent transgene dissemination, and do not teach the method steps; thus one would lack the motivation and reasonable expectation of success (response pg 13-14).

This is not found persuasive because the 35 USC 103 rejection was not maintained; the prior Office action merely addressed Applicant's arguments with respect to Fabijanski et al to the extent they would apply to the instant rejection.

12. Claims 19 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Metz et al (1995, Mol. Breed. 1:309-317).

Metz et al teach transformation of cytoplasmically sterile *Brassica oleracea* plants (Table 1). These plants are inherently unable to transmit the transgene via pollen. Broccoli would be cultivated for seed production for planting. As Metz et al teach all the method steps of the instant claims, Metz et al inherently teach the instantly claimed method. Additionally, Metz et al teach that the advantage of transforming male-sterile lines is that there is no danger of gene transfer to other plants through pollen (pg 315, right column, paragraph 3). The Bt gene encodes a compound that would be therapeutic or prophylactic for the plant.

Claim Rejections - 35 USC § 103

13. Claims 19 and 21-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over each of D'Halluin et al (US Patent 5,712,135, filed June, 1995) and Metz et al (1995, Mol. Breed. 1:309-317) in view of Welter (WO 98/06861).

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The claims are drawn to methods of transforming plants with constructs comprising an AMS gene and a collagen gene, with the goal of preventing spread of the collagen gene by pollen.

D'Halluin et al disclose transformation of maize with a male-sterility gene linked to a transgene of interest, the kanamycin resistance gene or the bar gene (column 19, line 47, to column 23, line 36). The kanamycin resistance gene and the bar gene encode compounds that are therapeutic or prophylactic for the plant. D'Halluin et al do not disclose transformation with a gene encoding collagen.

The teachings of Metz et al are discussed above. Metz et al do not disclose transformation with a gene encoding collagen.

Welter teaches the transformation of plants, including corn, broccoli and tomato, with the gene encoding collagen (claims 1-3, 6-7 and 9-12).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of transformation as taught by each of D'Halluin et al and Metz et al to transform the plants with a gene encoding collagen. One of ordinary skill in the art would have been motivated to do so because of the teachings of Metz et al that the advantage of transforming male-sterile lines is that there is no danger of gene transfer to other plants through pollen (pg 315, right column, paragraph 3) and the suggestion of D'Halluin et al to transform the plants with economically important proteins (column 10, lines 43-46).

14. Claims 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Metz et al (1995, Mol. Breed. 1:309-317) in view of Vedel et al (1994, Plant Physiol. Biochem. 32:601-618).

The claims are drawn to methods of transforming CMS *B napus* and maize plants with

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constructs comprising a transgene, with the goal of preventing spread of the gene by pollen.

The teachings of Metz et al are discussed above. Metz et al do not disclose CMS *B napus* or maize plants.

Vedel et al teach CMS *B napus* and maize plants (Table 3).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of transforming CMS plants with constructs comprising a transgene, with the goal of preventing spread of the gene by pollen, as taught by Metz et al to CMS *B napus* and maize plants as described in Vedel et al. One of ordinary skill in the art would have been motivated to do so because Metz et al teach that the advantage of transforming male-sterile lines is that there is no danger of gene transfer to other plants through pollen (pg 315, right column, paragraph 3).

Conclusion

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.

May 22, 2003

